Peer Review File

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Reviewer A

Good Job reviewing your patients for a significant problem. Consider evaluating patient's aTNF therapeutic drug level.
Reply 1: Thanks for your advice. In this study, therapeutic drug monitoring was conducted for 34 CD patients at the 14th week of IFX treatment.
Changes in the text: In this study, therapeutic drug monitoring was performed on 34 patients with CD at the 14th week of IFX treatment. Among them, 6 patients were in the secondary LOR group and 28 patients in the responder group. Results indicated that the IFX concentration at week 14 in the secondary LOR group was significantly lower than that in the responder group [(2.550±1.532) ug/ml vs. (6.654±4.801) ug/ml, t=3.724, P=0.001]. Due to low IFX concentrations, 16 CD patients chose to increase IFX dosage, or shorten the IFX administration interval, or combine with immunosuppressants to enhance IFX efficacy. We have modified our text as advised (see Page7 line3).

In this study, results demonstrated that the IFX concentration at week 14 of treatment in the secondary LOR group was significantly lower than that in the responder group. This finding supports an association between drug concentration and secondary LOR. We have modified our text as advised (see Page9 line7).

Reviewer B

The participant selection date ends December 2022, but observation end points were December 2023. Please clarify. It would be clinically useful to know which immunomodulator has the greatest protective effect for reducing secondary LOR.
Reply 2: Thanks for your advice. The participant selection date ends December 2022. To observe over an extended period whether secondary LOR occurred during IFX maintenance therapy, the follow-up period was extended until December 2023. Among the 69 CD patients in this study, 39 patients had not received combined immunomodulator therapy for more than 6 months, 23 patients had received combined azathioprine therapy for more than 6 months, and 7 patients had received combined methotrexate therapy for more than 6 months. Results showed no significant difference in the secondary LOR rate among the three groups (13/39 vs. 4/23 vs. 1/7, χ^2=4.401，P=0.111). However, the small sample size of this study introduces certain limitations. In future, large-sample studis will be needed to clarify the efficacy of different combined treatment regimens.
Changes in the text: However, it remains unclear which immunosuppressant achieves the optimal effect when combined with IFX. A network meta-analysis and systematic review indicated that no statistically significant differences were observed between various IFX-containing combination therapies in terms of inducing and maintaining remission in CD. Thus, additional head-to-head trials are warranted to address this question. We have modified our text as advised (see Page11 line14).